CHOATE

CHOATE HALL & STEWART LLP

Fax

CONFIDENTIAL

Recipient	Company	Fax	Phone
Examiner Karen A. Canella	USPTO	(571) 273-0828	(571) 272-0828
Mail Stop RCE	USPTO	(571) 273-8300	

From	Nadège M. Lagneau, Ph.D.	**Number of Pages**	32 (including this page)
Date	August 23, 2006	**Client Number**	2003080-0054
Phone	(617) 248-5150	**Operator**	**Time Sent**

Comments

Applicant: Danishefsky, *et. al.*
Examiner: Canella, Karen A.
Serial No: 09/641,742
Group Art Unit: 1643
Filing Date: August 18, 2000
Title: NOVEL GLYCOCONJUGATES, GLYCOAMINO ACIDS, INTERMEDIATES THERETO, AND USES THEREOF

In response to the Advisory Action mailed July 14, 2006, for the above-identified patent application, enclosed are:

(1) Transmittal (1 pg);
(2) Submission Under 37 C.F.R. §1.114 (27 pp);
(3) Request for Continued Examination Transmittal (1 pg);
(4) Petition for One Month's Extension of Time (1 pg);
(5) Credit Card Payment Form in the amount of $455.00 ($395 for RCE fee and $60 for Extension of Time Fee) (1 pg); and
(6) This Facsimile Cover Page (1 pg).

Respectfully submitted,

Nadège M. Lagneau, Ph.D.
Reg. No. 51,908

Return by Inter-office Mail Hold for pick-up

ATTORNEY'S DOCKET NUMBER: 2003080-0054 (SK-893-US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Danishefsky, *et al.*	Examiner:	Canella, Karen A.
Serial No.:	09/641,742	Art Unit:	1643
Filing Date:	August 18, 2000	Conf. No:	7338
Title:	NOVEL GLYCOCONJUGATES, GLYCOAMINO ACIDS, INTERMEDIATES THERETO, AND USES THEREOF		

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of Facsimile Transmission
Pursuant to 1096 OG 30-31

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent & Trademark Office (571) 273-8300 & (571) 273-0828 on the date indicated below.

August 23, 2006
Date

Signature

Mary Wilson
Typed or Printed Name of person signing certificate

Sir:

TRANSMITTAL LETTER

Enclosed for filing in the above-referenced patent application, please find the following documents:

1. Request for Continued Examination (RCE) (1 pg);
2. Submission Under 37 C.F.R. §1.114 (27 pp);
3. Petition for One Month's Extension of Time (1 pg);
4. Credit Card Payment Form in the amount of $455.00 ($395 for RCE fee and $60 for Extension of Time Fee) (1 pg); and
5. Facsimile Cover Sheet.

Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully Submitted,
CHOATE, HALL & STEWART LLP

Date: August 23, 2006

Nadège M. Lagneau, Ph.D.
Reg. No. 51,908

PATENT DEPARTMENT
CHOATE, HALL & STEWART LLP
Two International Place
Boston, Massachusetts 02110
Telephone: (617) 248-5000
Facsimile: (617) 248-4000

U.S.S.N: 09/641,742
4116184v1

Attorney Docket No.: 2003080-0054
Client Reference No.: ck-893-US

CHOATE

CHOATE HALL & STEWART LLP

Fax

CONFIDENTIAL

Recipient	Company	Fax	Phone
Examiner Karen A. Canella	USPTO	(571) 273-0828	(571) 272-0828
Mail Stop RCE	USPTO	(571) 273-8300	

From	Nadège M. Lagneau, Ph.D.	**Number of Pages**	32 (including this page)
Date	August 23, 2006	**Client Number**	2003080-0054
Phone	(617) 248-5150	**Operator**	**Time Sent**

Comments

Applicant: Danishefsky, *et. al.* Examiner: Canella, Karen A.
Serial No: 09/641,742 Group Art Unit: 1643
Filing Date: August 18, 2000
Title: NOVEL GLYCOCONJUGATES, GLYCOAMINO ACIDS, INTERMEDIATES THERETO, AND USES THEREOF

In response to the Advisory Action mailed July 14, 2006, for the above-identified patent application, enclosed are:

(1) Transmittal (1 pg);
(2) Submission Under 37 C.F.R. §1.114 (27 pp);
(3) Request for Continued Examination Transmittal (1 pg);
(4) Petition for One Month's Extension of Time (1 pg);
(5) Credit Card Payment Form in the amount of **$455.00** ($395 for RCE fee and $60 for Extension of Time Fee) (1 pg); and
(6) This Facsimile Cover Page (1 pg).

Respectfully submitted,

Nadège M. Lagneau, Ph.D.
Reg. No.: 51,908

Return by Inter-office Mail Hold for pick-up

ATTORNEY'S DOCKET NUMBER: 2003080-0054 (SK-893-US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Danishefsky, *et al.*	Examiner:	Canella, Karen A.
Serial No.:	09/641,742	Art Unit:	1643
Filing Date:	August 18, 2000	Conf. No:	7338
Title:	NOVEL GLYCOCONJUGATES, GLYCOAMINO ACIDS, INTERMEDIATES THERETO, AND USES THEREOF		

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of Facsimile Transmission
Pursuant to 1096 OG 30-31

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent & Trademark Office (571) 273-8300 & (571) 273-0828 on the date indicated below.

August 23, 2006
Date

Signature

Mary Wilson
Typed or Printed Name of person signing certificate

Sir:

TRANSMITTAL LETTER

Enclosed **for filing** in the above-referenced patent application, please find the following documents:

1. Request for Continued Examination (RCE) (1 pg);
2. Submission Under 37 C.F.R. §1.114 (27 pp);
3. Petition for One Month's Extension of Time (1 pg);
4. Credit Card Payment Form in the amount of **$455.00** ($395 for RCE fee and $60 for Extension of Time Fee) (1 pg); and
5. Facsimile Cover Sheet.

Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully Submitted,
CHOATE, HALL & STEWART LLP

Date: August 23, 2006

Nadège M. Lagneau, Ph.D.
Reg. No. 51,908

PATENT DEPARTMENT
CHOATE, HALL & STEWART LLP
Two International Place
Boston, Massachusetts 02110
Telephone: (617) 248-5000
Facsimile: (617) 248-4000

U.S.S.N: 09/641,742
4116184v1

Attorney Docket No.: 2003080-0054
Client Reference No.: ck-893-US

PTO-2038 (02-2003)
Approved for use through 02/28/2006. OMB 0651-0043
United States Patent and Trademark Office; U S DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

United States Patent and Trademark Office

Credit Card Payment Form

Please Read Instructions before Completing this Form

Credit Card Information

Credit Card Type: ☐ Visa ☐ MasterCard ☒ American Express ☐ Discover

Credit Card Account #: [redacted]006

Credit Card Expiration Date: February 2007

Name as it Appears on Credit Card: Lisa Walsh

Payment Amount: $(US Dollars): $455.00

Cardholder Signature: Lisa Walsh Date: August 23, 2006

Refund Policy: The Office may refund a fee paid by mistake or in excess of that required. A change of purpose after the payment of a fee will not entitle a party to a refund of such fee. The office will not refund amounts of $25.00 or less unless a refund is specifically requested, and will not notify the payor of such amounts (37 CFR § 1.26). Refund of a fee paid by credit card will be issued as a credit to the credit card account to which the fee was charged.

Service Charge: There is a $50.00 service charge for processing each payment refused (including a check returned "unpaid") or charged back by a financial institution (37 CFR § 1.21 (m)).

Credit Card Billing Address

Street Address 1: Choate, Hall & Stewart LLP

Street Address 2: Two International Place

City: Boston

State/Province: MA Zip/Postal Code: 02110

Country: U S

Daytime Phone #: 617-248-5000 Fax #: 617-248-4000

Request and Payment Information

Description of Request and Payment Information:

Extension of Time fee and RCE fee

☒ Patent Fee	☐ Patent Maintenance Fee	☐ Trademark Fee	☐ Other Fee
Application No 09/641,742	Application No	Application No	IDON Customer No
Patent No	Patent No	Registration No.	
Attorney Docket No 2003080-0054		Identify or Describe Mark	

If the cardholder includes a credit card number on any form or document other than the Credit Card Payment Form, the United States Patent and Trademark Office will not be liable in the event that the credit card number becomes public knowledge.

ATTORNEY'S DOCKET NUMBER: 2003080-0054 (SK-893-US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Danishefsky, *et al.*	Examiner:	Canella, Karen A.
Serial No.:	09/641,742	Art Unit:	1643
Filing Date:	August 18, 2000	Conf. No:	7338
Title:	NOVEL GLYCOCONJUGATES, GLYCOAMINO ACIDS, INTERMEDIATES THERETO, AND USES THEREOF		

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of Facsimile Transmission
Pursuant to 1096 OG 30-31

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent & Trademark Office (571) 273-8300 & (571) 273-0828 on the date indicated below.

August 23, 2006
Date

Signature

Mary Wilson
Typed or Printed Name of person signing certificate

Sir:

SUBMISSION UNDER 37 C.F.R. § 1.114

The present Submission is being submitted along with a Request for Continued Examination (RCE) Transmittal for the above-referenced case. A Final Office Action issued on April 25, 2006 in the present case. Applicant filed a Response on June 23, 2006. An Advisory Action issued on July 14, 2006. The shortened statutory deadline for replying to the Final Office Action of record was July 25, 2006. Applicant hereby requests a one-month extension of time extending the time for reply from July 25, 2006 to and including August 25, 2006. Therefore, Applicant respectfully submits that the filing of this Submission on August 23, 2006 is timely.

Applicant respectfully requests consideration of the following Remarks:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this Response.

Remarks begin on page 21 of this Response.

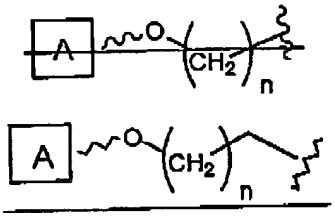
Conclusions begin on page 27 of this Response.

AMENDMENTS TO THE CLAIMS

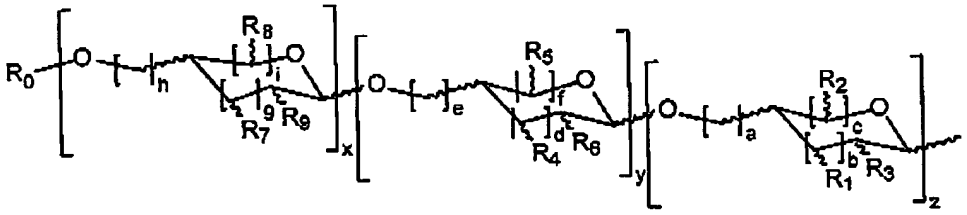
This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-55: Canceled

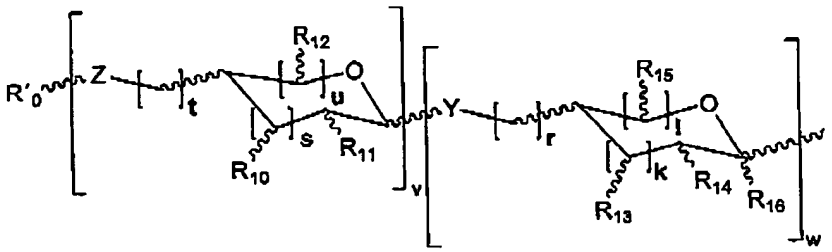
56. **(Currently Amended)** A multi-antigenic glycopeptide comprising a peptidic backbone made up of at least three amino acid residues, wherein two or more of said amino acids is independently substituted with a glycosidic moiety having the structure:



wherein each occurrence of A is a carbohydrate determinant having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that the x, y and z bracketed structures represent pyranose moieties and the sum of b and c is 2, the sum of d and f is 2, and the sum of g and i is 2, and with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 is independently hydrogen, OH, OR^i, NHR^i, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R^i is independently hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; with the proviso that the v and w bracketed structures represent pyranose moieties and the sum of l and k is ~~1 or~~ 2, and the sum of s and u is ~~1 or~~ 2, and with the proviso that v and w are not simultaneously 0; wherein R'_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} is independently hydrogen, OH, OR^{iii}, NHR^{iii}, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein each occurrence of R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group; and wherein each occurrence of R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

wherein each occurrence of ~~n is independently 0-9~~ n is independently 1-8 and ~~, whereby, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A.

57. **(Canceled)**

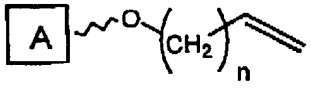
58. **(Previously Presented)** The glycopeptide of claim 56 wherein the glycopeptide is bound to an immunostimulant carrier protein, peptide or lipid.

59. **(Previously Presented)** The glycopeptide of claim 58 wherein the carrier protein is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

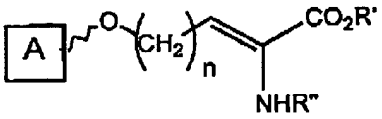
60. **(Previously Presented)** The glycopeptide of claim 58 wherein the lipid is tripalmitoyl-S-glycerylcysteinylserine.

61. **(Currently Amended)** The glycopeptide of claim 56 wherein the amino acids substituted with an n-alkyl glycosidic moiety are prepared by a process comprising steps of:

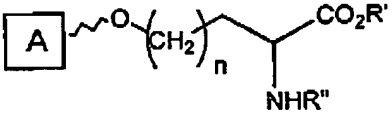
(a) providing an alkenyl glycoside having the structure:



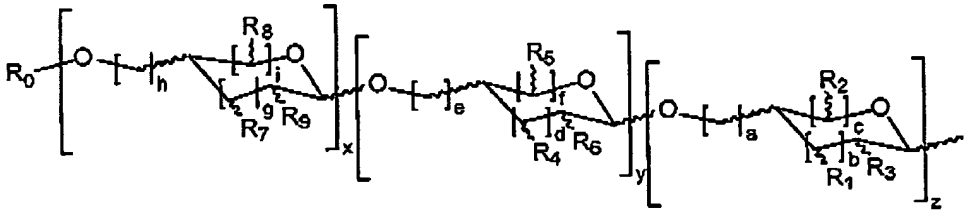
and reacting said alkenyl glycoside under suitable conditions to generate an enamide ester having the structure:



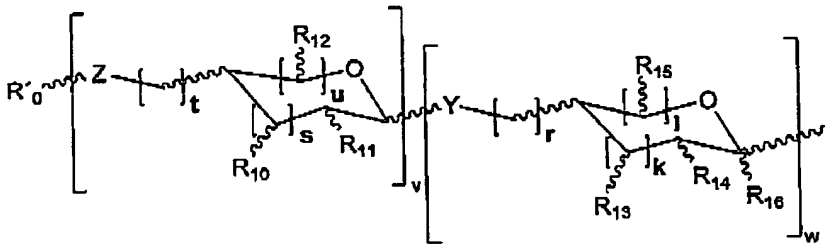
(b) reacting said enamide ester under suitable conditions to generate a glycoamino acid having the structure:



wherein, for each of the structures above, ~~n is 0-9~~ n is 1-8, wherein A is a carbohydrate domain having the structure:



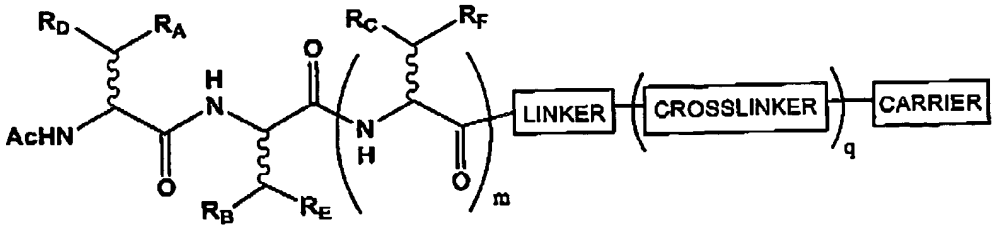
wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that the x, y and z bracketed structures represent pyranose moieties and the sum of b and c is 2, the sum of d and f is 2, and the sum of g and i is 2, and with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 is independently hydrogen, OH, OR^i, NHR^i, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R^i is independently hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; with the proviso that the v and w bracketed structures represent pyranose moieties and the sum of l and k is ~~1 or~~ 2, and the sum of s and u is ~~1 or~~ 2, and with the proviso that v and w are not simultaneously 0; wherein R'_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} is independently hydrogen, OH, OR^{iii}, NHR^{iii}, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein each occurrence of R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group; and wherein each occurrence of R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

and wherein for the glycoamino acid structure R' and R" are each independently protecting group or hydrogen.

62. **(Currently Amended)** The glycopeptide of claim 56, wherein said glycopeptide is a construct having the structure:



wherein the linker is -O-, $-NR_G-$, $-NR_G(CR_HR_I)_kNR_J-$, $-NR_G(CR_HR_I)_kNR_J(C=O)(CR_HR_I)_kS-$, $-(CR_HR_J)_kNR_I-$, $-O(CR_HR_I)_kNR_J$, an oligoester fragment comprising from 2 to about 20 hydroxy acyl residues, a peptidic fragment comprising from 2 to about 20 amino acyl residues, or a linear or branched chain alkyl or aryl carboxylic ester; wherein each occurrence of k is independently 1-5; and each occurrencence of R_G, R_H, R_I and R_J is independently hydrogen, a linear or branched, substituted or unsubstituted, cyclic or acyclic alkyl moiety, or a substituted or unsubstituted aryl moiety;

wherein the crosslinker is a moiety derived from a crosslinking reagent capable of conjugating a surface amine of the carrier with a terminal thiol of the linker;

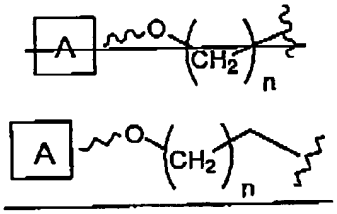
wherein the carrier is a protein or lipid;

wherein m is 1, 2 or 3;

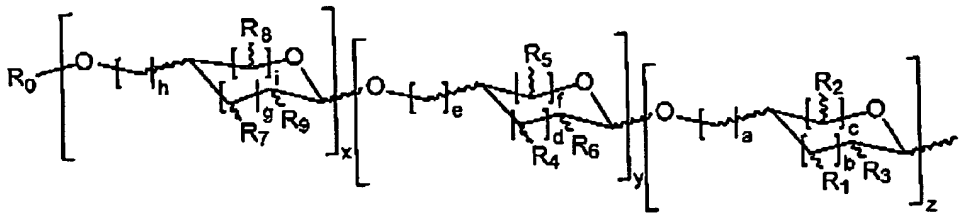
wherein q is 0 or 1;

wherein each occurrence of R_A, R_B and R_C is independently H or methyl; and

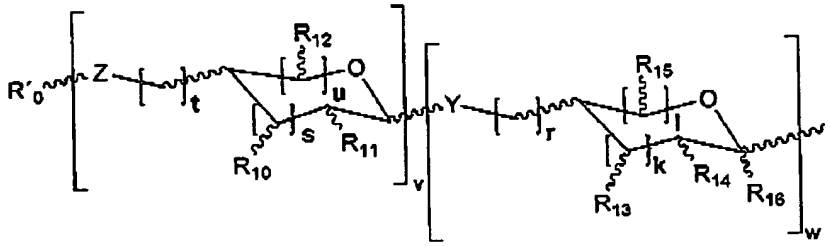
wherein each occurrence of R_D, R_E and R_F is independently an alkyl glycosidic moiety having the structure:



wherein each occurrence of A is independently selected from a carbohydrate domain having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that R_D, R_E and R_F are carbohydrates independently comprised of pyranose moieties, and the sum of b and c is 2, the sum of d and f is 2, and the sum of g and i is 2, and with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 is independently hydrogen, OH, OR^i, NHR^i, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R^i is independently hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; with the proviso that the v and w bracketed structures represent pyranose moieties and the sum of l and k is ~~1 or~~ 2, and the sum of s and u is ~~1 or~~ 2, and with the proviso that v and w are not simultaneously 0; wherein R'_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} is independently hydrogen, OH, OR^{iii}, NHR^{iii}, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein each occurrence of R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted

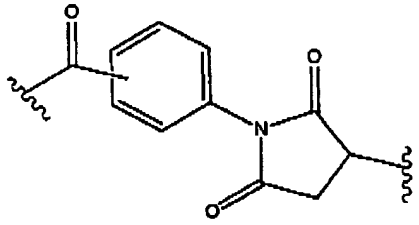
linear or branched chain alkyl, acyl, arylalkyl or aryl group; and wherein each occurrence of R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

wherein each occurrence of ~~n is independently 0-9~~ n is independently 1-8; ~~, whereby, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

63. **(Canceled)**

64. **(Canceled)**

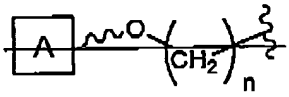
65. **(Previously Presented)** The construct of claim 62, wherein the crosslinker is a fragment having the structure:

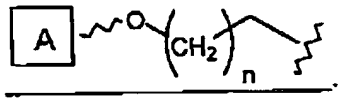


whereby said structure is generated upon conjugation of maleimidobenzoic acid N-hydroxy succinimide ester with a linker.

66. **(Previously Presented)** The construct of claim 62, wherein m is 1 and the construct has three occurrences of A comprising Tn, Globo-H and Le^y.

67. **(Currently Amended)** The glycopeptide of claim 56 wherein the glycopeptide has six occurrences of the alkyl glycosidic moiety having the structure:





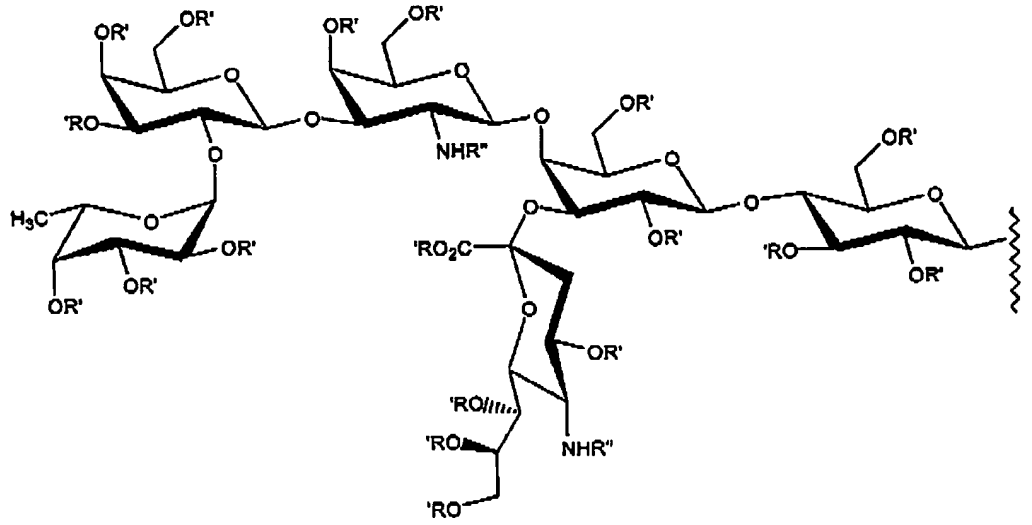
68. **(Canceled)**

69. **(Previously Presented)** The glycopeptide of claim 56 or 67 or the construct of claim 62, wherein each occurrence of A is independently Globo-H, fucosyl GM1, KH-1, glycophorin, STN, Le^y, N3, Tn, 2,6-STn, (2,3)ST, or TF.

70. **(Previously Presented)** The construct of claim 62 wherein the carrier is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

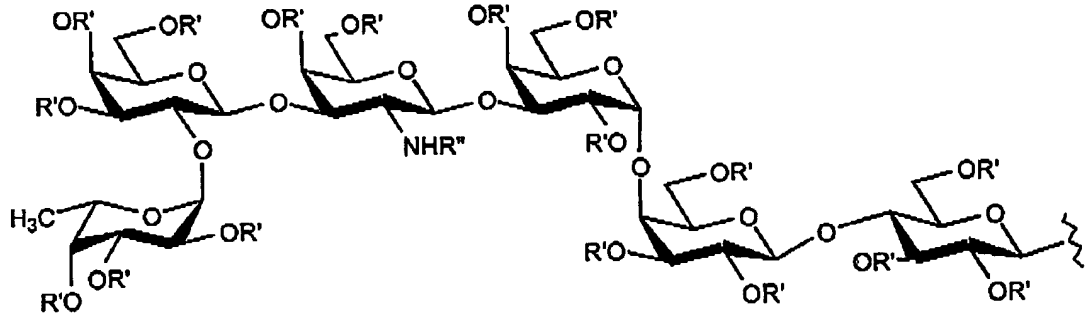
71. **(Previously Presented)** The construct of claim 62 wherein the carrier is tripalmitoyl-S-glycerylcysteinylserine.

72. **(Previously Presented)** The glycopeptide of claim 56 or 67 or the construct of claim 62, wherein at least one occurrence of A is a carbohydrate determinant having the structure:



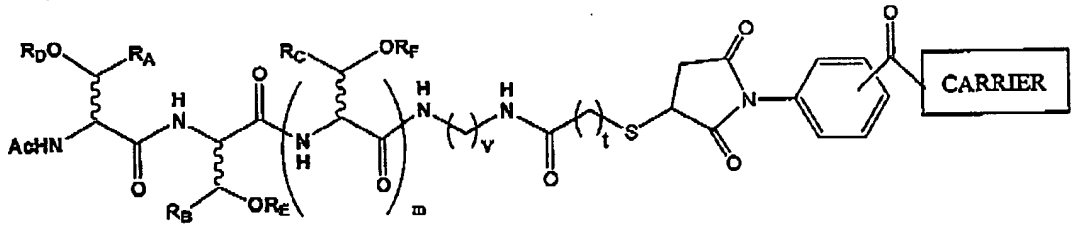
wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein each occurrence of R′′ is independently hydrogen or a nitrogen protecting group.

73. **(Previously Presented)** The glycopeptide of claim 56 or 67 or the construct of claim 62, wherein at least one occurrence of A is a carbohydrate determinant having the structure:



wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein R′′ is hydrogen or a nitrogen protecting group.

74. **(Currently Amended)** The construct of claim 62 having the structure:



wherein R_A, R_B and R_C are each independently H or methyl;

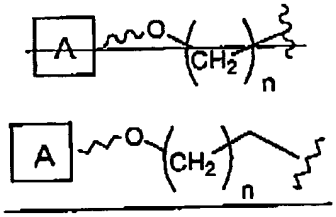
m is 1, 2 or 3;

v is 1-8;

t is 1-8; and

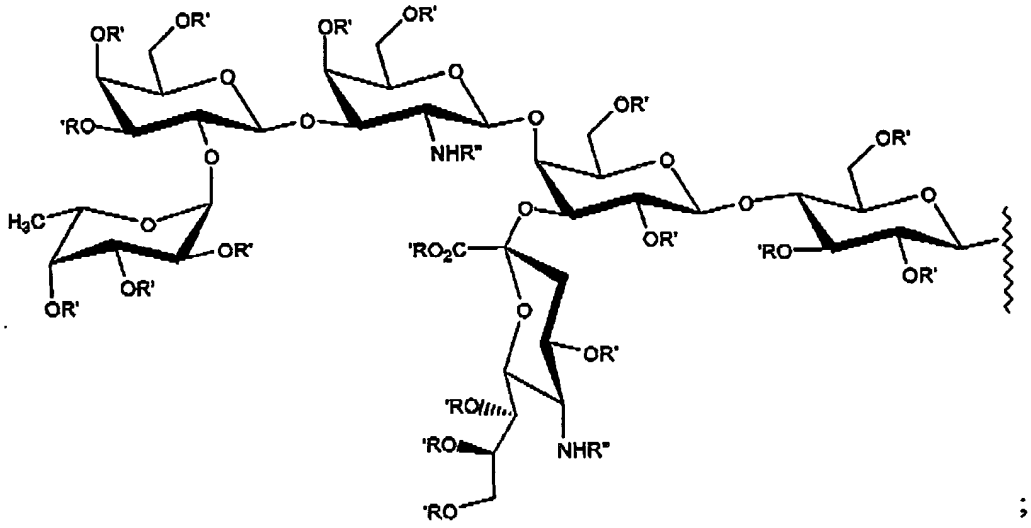
the carrier is a protein;

wherein each occurrence of R_D, R_E and R_F is independently an alkyl glycosidic moiety having the structure:



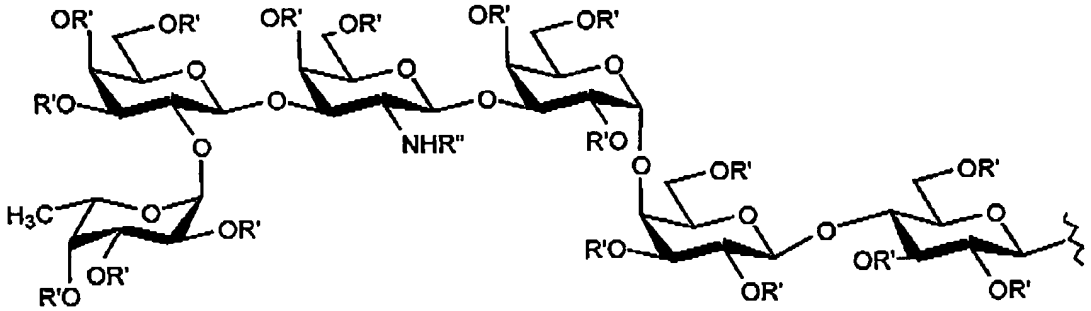
wherein ~~n is 0-9~~ n is 1-8;

each occurrence of A is independently a carbohydrate domain selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, STN, Le^y, N3, Tn, 2,6-STn, (2,3)ST, or TF, a carbohydrate domain having the structure:



;

or a carbohydrate domain having the structure:



;

wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein R′′ is hydrogen or a nitrogen protecting group

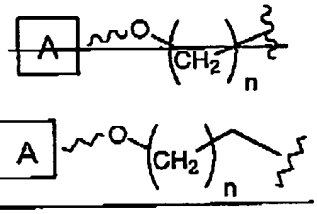
whereby~~, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

75. **(Previously Presented)** The construct of claim 74, wherein the protein is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

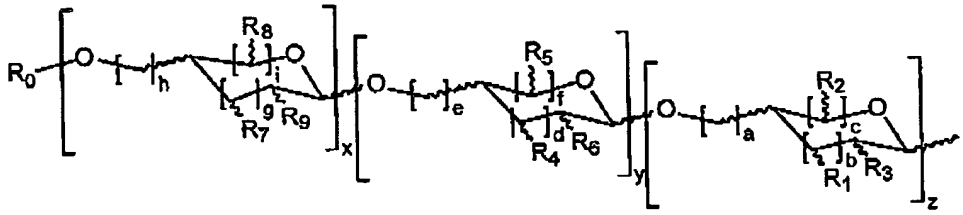
76. **(Currently Amended)** A pharmaceutical composition comprising:

one or more immunological adjuvants and/or a pharmaceutically suitable carrier; and

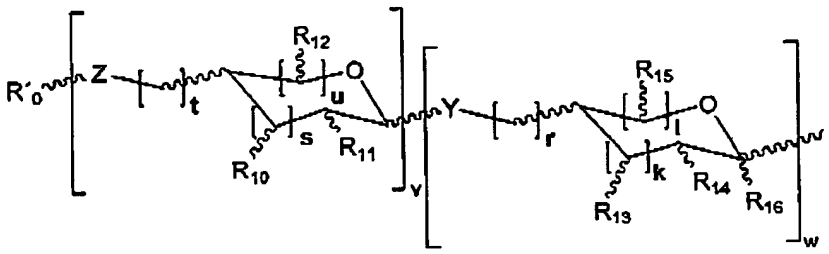
a multi-antigenic glycopeptide comprising a peptidic backbone made up of at least three amino acid residues, wherein two or more of said amino acids is independently substituted with a glycosidic moiety having the structure:



wherein each occurrence of A is a carbohydrate determinant having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that the x, y and z bracketed structures represent pyranose moieties and the sum of b and c is 2, the sum of d and f is 2, and the sum of g and i is 2, and with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 is independently hydrogen, OH, OR^i, NHR^i, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R^i is independently hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; with the proviso that the v and w bracketed structures represent pyranose moieties and the sum of l and k is ~~1 or~~ 2, and the sum of s and u is ~~1 or~~ 2, and with the proviso that v and w are not simultaneously 0; wherein R'_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} is independently hydrogen, OH, OR^{iii}, NHR^{iii}, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein each occurrence of R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group; and wherein each occurrence of R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

wherein each occurrence of ~~n is independently 0-9~~ n is independently 1-8 and~~, whereby, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A.

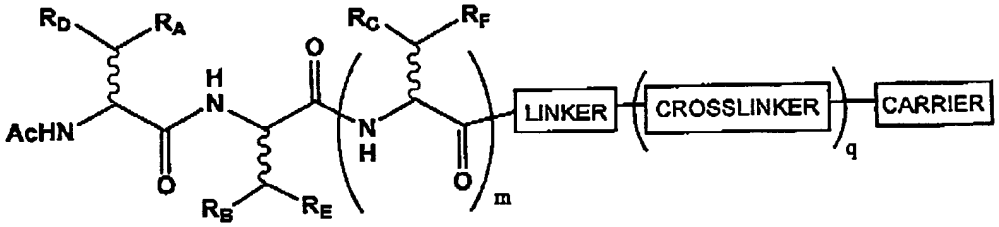
77. **(Canceled)**

78. **(Previously Presented)** The pharmaceutical composition of claim 76 wherein the glycopeptide is bound to an immunostimulant carrier protein or lipid.

79. **(Previously Presented)** The pharmaceutical composition of claim 78 wherein the carrier protein is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

80. **(Previously Presented)** The pharmaceutical composition of claim 78 wherein the lipid is tripalmitoyl-S-glycerylcysteinylserine.

81. **(Currently Amended)** The pharmaceutical composition of claim 76, wherein said glycopeptide is a construct having the structure:



wherein the linker is -O-, $-NR_G-$, $-NR_G(CR_HR_I)_kNR_J-$, $-NR_G(CR_HR_I)_kNR_J(C=O)(CR_HR_I)_kS-$, $-(CR_HR_J)_kNR_J-$, $-O(CR_HR_I)_kNR_J$, an oligoester fragment comprising from 2 to about 20 hydroxy acyl residues, a peptidic fragment comprising from 2 to about 20 amino acyl residues, or a linear or branched chain alkyl or aryl carboxylic ester; wherein each occurrence of k is independently 1-5; and each occurrencence of R_G, R_H, R_I and R_J is independently hydrogen, a linear or branched, substituted or unsubstituted, cyclic or acyclic alkyl moiety, or a substituted or unsubstituted aryl moiety;

wherein the crosslinker is a moiety derived from a crosslinking reagent capable of conjugating a surface amine of the carrier with a terminal thiol of the linker;

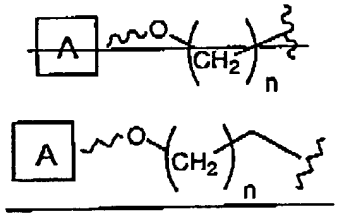
wherein the carrier is a protein or lipid;

wherein m is 1, 2 or 3;

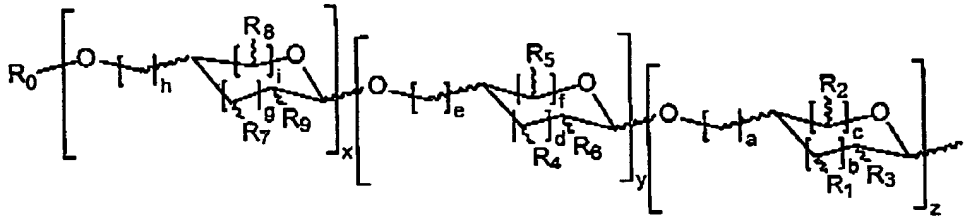
wherein q is 0 or 1;

wherein each occurrence of R_A, R_B and R_C is independently H or methyl; and

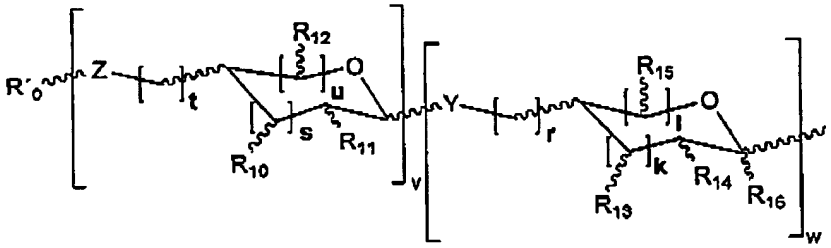
wherein each occurrence of R_D, R_E and R_F is independently an alkyl glycosidic moiety having the structure:



wherein each occurrence of A is independently selected from a carbohydrate domain having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that R_D, R_E and R_F are carbohydrates independently comprised of pyranose moieties, and the sum of b and c is 2, the sum of d and f is 2, and the sum of g and i is 2, and with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 is independently hydrogen, OH, OR^i, NHR^i, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R^i is independently hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; with the proviso that the v and w bracketed structures represent pyranose moieties and the sum of l and k is ~~1 or~~ 2, and the sum of s and u is ~~1 or~~ 2, and with the proviso that v and w are not simultaneously 0; wherein R'_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein each occurrence of R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} is independently hydrogen, OH, OR^{iii}, NHR^{iii}, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein each occurrence of R_{16} is hydrogen, COOH,

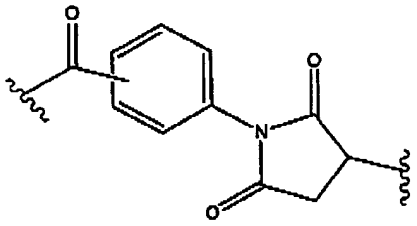
$COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein each occurrence of R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, acyl, arylalkyl or aryl group; and wherein each occurrence of R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

wherein each occurrence of ~~n is independently 0-9~~ n is independently 1-8 and~~, whereby, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

82. **(Canceled)**

83. **(Canceled)**

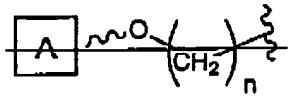
84. **(Previously Presented)** The pharmaceutical composition of claim 81, wherein the crosslinker is a fragment having the structure:

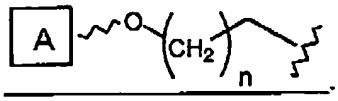


whereby said structure is generated upon conjugation of maleimidobenzoic acid N-hydroxy succinimide ester with a linker.

85. **(Previously Presented)** The pharmaceutical composition of claim 81, wherein m is 1 and the construct has three occurrences of A comprising Tn, Globo-H and Le^y.

86. **(Previously Presented)** The pharmaceutical composition of claim 76, wherein the glycopeptide has six occurrences of the alkyl glycosidic moiety having the structure:





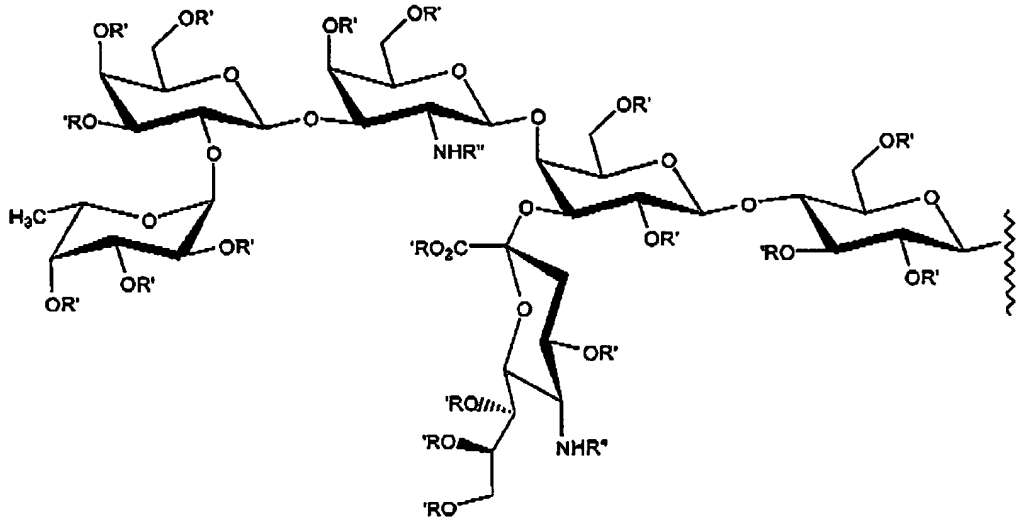
87. **(Canceled)**

88. **(Previously Presented)** The pharmaceutical composition of claim 76, 81 or 86, wherein each occurrence of A is independently Globo-H, fucosyl GM1, KH-1, glycophorin, STN, Le^y, N3, Tn, 2,6-STn, (2,3)ST, or TF.

89. **(Previously Presented)** The pharmaceutical composition of claim 81 or 86 wherein the carrier is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

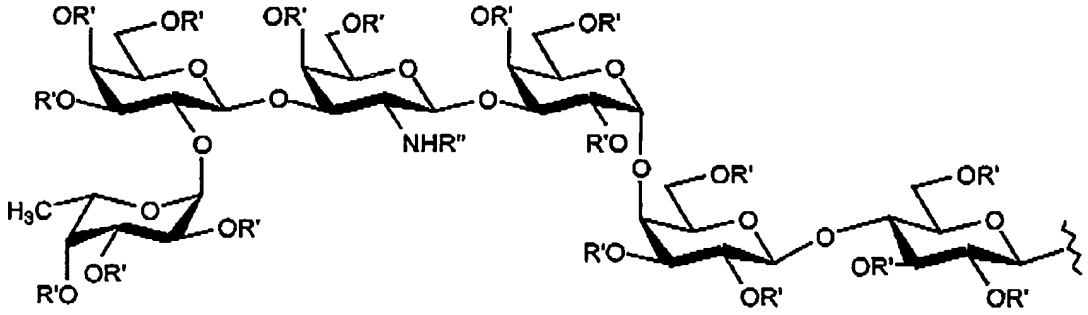
90. **(Previously Presented)** The pharmaceutical composition of claim 81 or 86 wherein the carrier is tripalmitoyl-S-glycerylcysteinylserine.

91. **(Previously Presented)** The pharmaceutical composition of claim 76, 81 or 86, wherein at least one occurrence of A is a carbohydrate determinant having the structure:



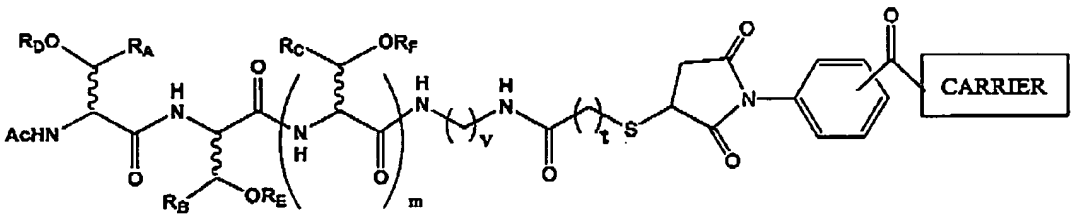
wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein each occurrence of R′′ is independently hydrogen or a nitrogen protecting group.

92. **(Previously Presented)** The pharmaceutical composition of claim 76, 81 or 86, wherein at least one occurrence of A is a carbohydrate determinant having the structure:



wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein R′′ is hydrogen or a nitrogen protecting group.

93. **(Currently Amended)** The pharmaceutical composition of claim 81, wherein the construct has the structure:



wherein R_A, R_B and R_C are each independently H or methyl;

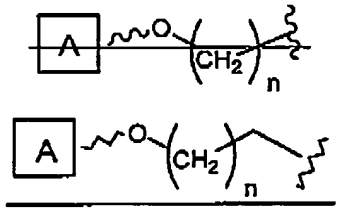
m is 1, 2 or 3;

v is 1-8;

t is 1-8; and

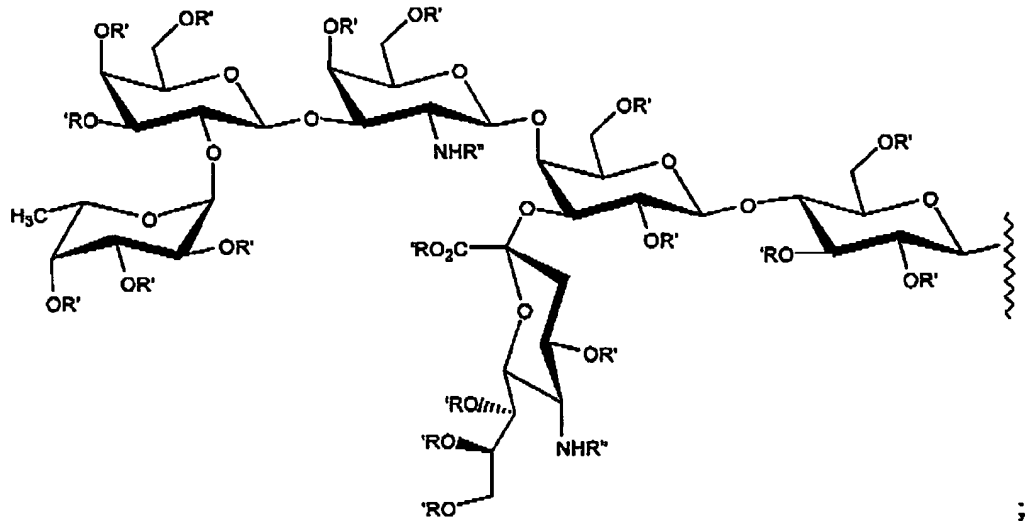
the carrier is a protein;

wherein each occurrence of R_D, R_E and R_F is independently an alkyl glycosidic moiety having the structure:



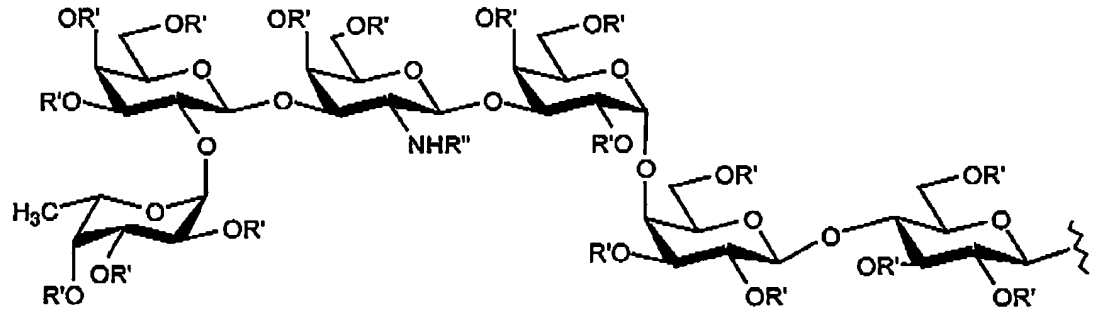
wherein ~~a is 0-9~~ n is 1-8;

each occurrence of A is independently a carbohydrate domain selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, STN, Le^y, N3, Tn, 2,6-STn, (2,3)ST, or TF, a carbohydrate domain having the structure:



;

or a carbohydrate domain having the structure:



;

wherein each occurrence of R′ is independently hydrogen or a protecting group; and wherein R″ is hydrogen or a nitrogen protecting group

whereby~~, if for each occurrence of n, n = 0,~~ at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

94. **(Previously Presented)** The pharmaceutical composition of claim 93, wherein the protein is bovine serum albumin, polylysine or keyhole limpet hemocyanin.

95. **(Previously Presented)** The pharmaceutical composition of claim 76 wherein at least one of said one or more immunological adjuvants is a saponin adjuvant.

96. **(Previously Presented)** The pharmaceutical composition of claim 95 wherein the saponin adjuvant is GPI-0100.

97. **(Previously Presented)** The pharmaceutical composition of claim 76 wherein at least one of said one or more immunological adjuvants is bacteria or liposomes.

98. **(Previously Presented)** The pharmaceutical composition of claim 97 wherein the immunological adjuvant is Salmonella minnesota cells, bacille Calmette-Guerin or QS21.

REMARKS

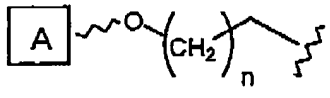
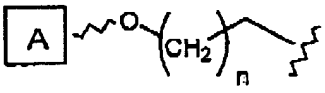
The Examiner issued an Advisory Action on July 14, 2006 in which she stated that Applicant's amendment filed June 23, 2006 would not be entered because it allegedly raised issues of new matter. A telephone interview between Examiner Canella and Applicant's representatives Brenda Herschbach Jarrell and Nadège Lagneau took place on August 22, 2006. The purpose of the interview was to orient the Examiner to the amendments filed with Applicant's 6/23/06 response, and to demonstrate that none of the amendments introduced new matter. The Examiner agreed that Applicant's amendments did not raise issues of new matter and stated that she would issue an interview summary to that effect. It was further agreed that Applicant would file this RCE to allow the Examiner an opportunity to fully consider the amendments and examine whether the claims, as amended, are allowable over the art of record.

1. Status of the Claims

Claims 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-98 are currently pending in the application. Claims 56, 58-62, 69, 76, 78-81, 88-90, 97 and 98 are rejected under 35 U.S.C. § 102(a) and/or 102(b) over Danishefsky *et al.* (Angew. Chem. Int. Ed., 2000, *39*, pp. 836-863), WO 99/48515 and Toyokuni *et al.* (Chemical Society Reviews, 1995, *24*, pp. 321-242). In addition, the claims are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over co-pending application Nos.: 10/209,618 and 10/728,041.

2. Amendments to the Claims

Claims 56, 61, 62, 67, 74, 76, 81 and 93 have been amended. Claims 58-60, 65-66, 69-73, 75, 78-80, 84-86, 88-92 and 94-98 remain unchanged. Applicant respectfully submits that no new matter is added through the proposed amendment to the claims. The proposed amendments are fully supported by the specification and claims, as originally filed.

Claims 56, 62, 67, 74, 76, 81 and 93, as amended, recite  as the alkyl glycosidic moiety wherein n is 1-8. Support for this amendment can be found throughout the specification, for example, in original claim 27, line 25 page 33, line 9 page 35, line 21 page 36 and line 12 page 38 where the moiety  is depicted.

In claim 27 and the specification, as originally filed, n was defined as an integer from 0-8 (See, for example, original claim 27, line 17 p. 11, line 9 p. 35, and line 11 p. 38 of the specification, as filed). In the instant claims, n is an integer ranging from 1-8. Specific support for n ranging between 1 and 8 can be found, for example, at lines 20-23 page 35 of the specification, as filed, where one aspect of the invention is identified as encompassing clustered glycopeptides *where n is greater than or equal to 1* (*i.e.*, n=1-8). Further support can be found, for example, in Figures 15 and 16, as filed.

Claim 61, as amended, recites n = 1-8. As discussed above, support for n ranging from 1-8 can be found, for example, at line 17 p. 11, line 9 p. 35, line 11 p. 38 and lines 20-23 page 35 of the specification, as filed.

In addition, claims 56, 61, 62, 76 and 81 have been amended to correct the value of the sums l and k, and s and u, in light of the fact that the v and w bracketed structures represent pyranose moieties.

Furthermore, claims 56, 62, 74, 76, 81 and 93 recite that "at least one occurrence of A has a different structure from other occurrences of A." This language is fully supported by the specification as filed. For example, support can be found at lines 20-23 p. 35 of the specification in the teaching that n-alkyl linked (where n is greater than or equal to 1) clustered glycopeptides *may incorporate multiple antigenic structures* or may also incorporate all of the same antigenic structures. Further support can be found, for example, in Figure 16 (Compound 54).

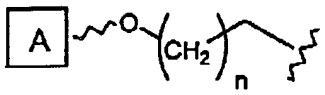
No new matter is being introduced by these amendments. Applicant is submitting the present amendments without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be lost by virtue of this paper, and explicitly reserves the right to pursue the subject matter of any of the canceled claims, or some or all of the subject matter which might be lost by virtue of this paper, in Divisional or Continuation Applications.

3. New matter rejections levied in the Examiner's Advisory Action dated July 14, 2006

The Examiner levied the following two new matter rejections against Applicant's claim amendment filed on June 23, 2006:

(a) First new matter rejection: The Examiner states that the new structural moiety in amended claim 56 presents new matter because it encompasses a different range of structures having at least two methylene group, in contrast to the limitation of the originally filed disclosure which permitted 0 to 9 methylene groups.

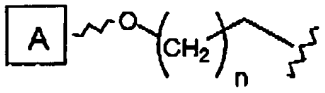
The new structural moiety that the Examiner is referring to is the n-alkyl glycosyl moiety:



where n =1-8. The amendment to claim 56 (as well as claims 62, 67, 74, 76, 81 and 93) introducing this n-alkyl glycosyl moiety was merely meant to ensure that the claim language was consistent with the specification, as filed (*i.e.*, to ensure that variable n was used consistently, and to avoid any possibility of confusion). The n-alkyl glycosyl moiety depicted in claim 56 (and claims 62, 67, 74, 76, 81 and 93) is identical to that depicted in original claim 27, and throughout the specification as originally filed (see, for example, line 25 page 33, line 9 page 35, line 21 page 36 and line 12 page 38 of the specification). Original claim 27 recited n=0-8. Therefore, the originally filed disclosure permits 1 to 9 methylene groups linking the antigen A to the peptidic backbone (not 0-9 as stated in the Advisory Action).

Claim 56 (and claims 62, 67, 74, 76, 81 and 93) differs from original claim 27 in that it recites n=1-8, instead of n=0-8 in original claim 27. However, the embodiment n=1-8 (as claimed in the instant claims) is specifically recited in the specification, as originally filed. Applicant points, for example, to lines 20-23 page 35 of the specification where one aspect of the invention is identified as encompassing clustered glycopeptides *where n is greater than or equal to 1* (*i.e.*, n=1-8). Further support can be found, for example, in Figures 15 and 16, in which glycopeptides are depicted where each carbohydrate determinant is attached to the peptidic backbone via an n-alkyl linker having more than one carbon atom (*i.e.*, $n \geq 1$).

Thus, no new matter is being introduced by reciting the n-alkyl glycosyl moiety:



where n =1-8 in claims 56 (and claims 62, 67, 74, 76, 81 and 93).

(b) Second new matter rejection: The Examiner states that the amendment to claim 74 broadens the claimed structures by deleting the requirement of having an alpha or beta linkage to an amino acid. The Examiner concludes that the amendment to claim 74 thus introduced new matter.

The amendment to claim 74 (as well as claims 62, 81 and 93) seeking to delete the language "wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid" was solely meant to remove what Applicant viewed as a redundant statement. During the telephonic interview of August 22, the Examiner agreed that the amendment did not introduce new matter.

However, the Examiner requested that the language be kept in the claims for clarity purposes, which Applicant has done in the present amendment.

Thus, there are no outstanding new matter issues in the amendment detailed herein.

4. Rejections under 35 U.S.C. § 102

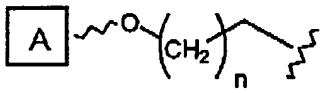
A. The Examiner has rejected claims 56, 58-61, 69, 76, 78-80, 88, 97 and 98 under 35 U.S.C. § 102 (a) as being anticipated by Danishefsky *et al.* (Angew. Chem. Int. Ed., 2000, ***39***, pp. 836-863). Specifically, the Examiner points to the structures on pages 855-859 of the cited reference and states that they anticipate the instant claims.

B. The Examiner has rejected claims 56, 58, 62, 69, 76, 78-81 and 88-90 under 35 U.S.C. § 102 (a) as being anticipated by WO 99/48515. Specifically, the Examiner points to compounds 3, 4 and 5 in Figure 20 of the cited reference (citing Figures 20A and 20C), and states that they anticipate the instant claims.

C. The Examiner has rejected claims 56, 61, 69, 76 and 78 under 35 U.S.C. § 102 (b) as being anticipated by Toyokuni *et al.* (Chemical Society Reviews, 1995, ***24***, pp. 321-242). Specifically, the Examiner points to compound 19 in Scheme 11 of the cited reference, and states that it anticipates the instant claims.

In all the glycopeptides referred to by the Examiner in each of the cited references, the antigen-bearing amino acid residues are substituted with a glycosidic moiety having the structure A-O-, which is attached to the peptidic backbone through <u>*one*</u> carbon atom. Furthermore, in the glycopeptides disclosed in the cited art, each occurrence of A is the same.

The claims, as amended herein, recite an alkyl glycosidic moiety having the structure



where n is 1-8. Accordingly, in the claimed glycopeptides, <u>*two or more*</u> carbon atoms separate the carbohydrate determinant A and the peptidic backbone. In addition, in the claimed multi-antigenic glycopeptides, <u>*at least one occurrence of the antigenic structure A has a different structure from other occurrences of A*</u>.

Therefore, the glycopeptides disclosed in the cited art are specifically excluded from the instant claims because, in the claimed multi-antigenic glycopeptides, n cannot be 0, and at least

one occurrence of the antigenic structure A has a different structure from other occurrences of A. Accordingly, the cited references cannot anticipate the present claims.

5. Additional comments

The instant claims are directed to multi-antigenic glycopeptides comprising two or more glycosidic moieties A-O-$(CH_2)_n$-CH_2-, wherein at least one occurrence of A has a different structure from other occurrences of A. Because the claimed glycopeptides comprise more than one type of carbohydrate antigen, they have superior properties over the glycopeptides disclosed in the cited art. It is well established that transformed cancerous cells exhibit abnormal cell surface glycosylation patterns. As stated in the specification, identified cancer carbohydrate antigens such as TF, Tn, sTN, KH-1, Le^y and Globo-H have been carefully characterized as being over-expressed at the surface of malignant cells in a variety of cancers (breast, colon, prostate, ovarian, liver, small cell lung and adenocarcinomas). Thus, the claimed glycopeptides have superior immunotherapeutic properties than the cited prior art glycopeptides, in that a single claimed glycopeptide can induce the production of more than one type of antibodies (*i.e.*, antibodies against the two or more types of carbohydrate antigens present on the glycopeptide). In Applicant's response of June 23, 2006, copies of several publications were provided demonstrating that multi-antigenic glycopeptides such as those claimed in the instant application can be used to induce antibodies against individual carbohydrate antigens present on the glycopeptide, which antibodies are reactive with one or more cancer cell lines expressing these antigens. See, for example, Ragupathi *et al.*, *J. Am. Chem. Soc.*, (2006), **128**, 2715-2725.

Copies of publications provided with Applicant's 6/23/06 response:

1. Allen *et al.*, *J. Am. Chem. Soc.*, (2001), **123**, 1890-1897.
2. Ragupathi *et al.*, *PNAS*, (2002), **99**(21), 13699-13704.
3. Keding *et al.*, *PNAS*, (2004), **101**(33), 11937-11942.
4. Ragupathi *et al.*, *J. Am. Chem. Soc.*, (2006), **128**, 2715-2725.

Copies of the above-references are not being re-submitted with the present RCE submission. Should the Examiner require replacement copies, please inform the undersigned, who will arrange for additional copies to be sent to the attention of the Examiner.

In addition, in the claimed multi-antigenic glycopeptides, each carbohydrate domain is attached to a *non-natural* amino acid residue (*i.e.*, n cannot be 1). In contrast, in the

glycopeptides disclosed in the cited art, each carbohydrate determinant A is attached to the peptidic backbone via a *natural* amino acid (Serine or Threonine). This difference (natural v. non-natural amino acids) is expected to impart different properties to the claimed glycoconjugates as compared to the glycopeptides disclosed in the cited art (in particular those containing long, aliphatic side chains (-$(CH_2)_nCH_2$-) which create a greater distance between the peptide backbone and the carbohydrate determinants), for example in terms of ease of their preparation and/or strength of immune response they induce.

Therefore, there is no subject matter overlap between the presently claimed invention and the cited art, nor is the claimed subject matter obvious over the cited art.

6. **Provisional Obviousness-type Double Patenting Rejection**

The Examiner has provisionally rejected claims 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-98 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 118-198 of co-pending application No.: 10/209,618 and claims 1-36 of co-pending application No.: 10/728,041. The Examiner states that the claims in the cited applications anticipate the instant claims (see page 8 of the Office Action mailed 10/12/2005).

Applicant notes that co-pending application No.: 10/728,041 filed December 3, 2003 is a continuation-in-part of co-pending patent application No.: 10/209,618 filed July 31, 2002; which is a continuation-in-part of the present application. Therefore, the '041 and '618 applications do not have an earlier effective filing date than the present application. Accordingly, the claims in the '041 and '618 applications cannot anticipate the present claims.

Applicant respectfully refrains from further commenting on this provisional rejection unless and until such time as it matures into an actual rejection. Application serial numbers 10/209,618 and 10/728,041 and the instant application are assigned to the same entity. Once application serial number 10/209,618 and/or 10/728,041 has been allowed, and if the allowed claims in 10/209,618 and/or 10/728,041 are not deemed patentably distinct from the allowed claims in the instant application, Applicant is prepared to file a terminal disclaimer in application serial number 10/209,618 and/or 10/728,041.

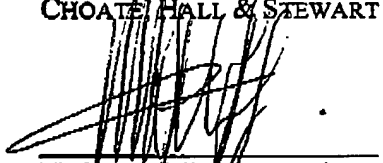
CONCLUSION

Applicant thanks Examiner Canella for her time and consideration. In light of the foregoing Remarks, Applicant respectfully submits that the present application is in condition for allowance; a Notice to that effect is respectfully requested.

If a telephone conversation would help clarify any issues, or help expedite prosecution of this case, Applicant invites the Examiner to contact the undersigned at (617) 248-5150.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those which may otherwise be provided for in documents accompanying this paper. However, in the event that any additional fees are required for consideration of this paper (including fees for net addition of claims), these fees are authorized to be charged to our Deposit Account No. 03-1721.

Respectfully submitted,
CHOATE, HALL & STEWART LLP



Date: August 23, 2006

Nadège M. Lagneau, Ph.D.
Reg. No.: 51,908

PATENT GROUP
CHOATE, HALL & STEWART, LLP
Two International Place
Boston, MA 02110
Telephone: 617-248-5150
Facsimile: 617-248-4000